

Appl. No. : 10/534,825  
Confirmation No. : 8880  
Applicant : David Edwin Thurston, et al.

Filed : October 20, 2005  
Title : Pyrrolobenzodiazepines

TC/A.U. : 1624  
Examiner : Bruck Kifle

Docket No. : 065435-9048-US00

Customer No. : 023510

Mail Stop AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 C.F.R. 1.132**

I, Dr. Philip Howard, declare as follows:

1. I have personal knowledge of the following facts and I make this declaration in support of the prosecution of U.S. Patent Application Serial No. 10/54,825 before the United States Patent and Trademark Office.

2. I am currently employed Vice-President (Chemistry) at SpiroGen Limited, a position I have held since June 2003 (full time). Prior to that I was employed as Senior Research Officer, University of London, School of Pharmacy.

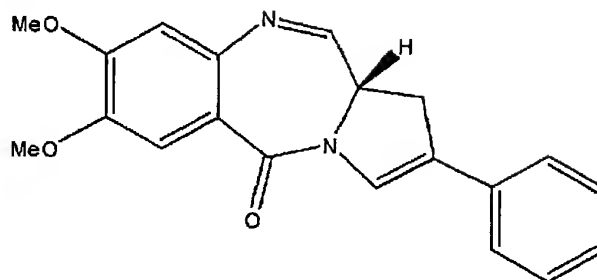
3. My curriculum vitae is attached as Appendix A.

4. I am a co-inventor of the subject matter of the above-identified application and I am familiar with the art and with the prosecution history of this application.

5. We have now performed additional comparative testing between the compounds of the present invention and the prior art compounds.

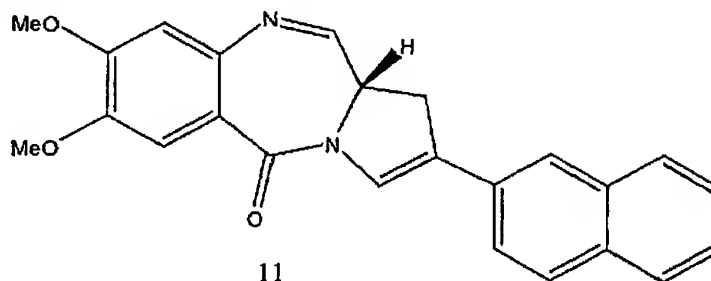
Appl. No. 10/534,825  
Amdt. dated September 4, 2007  
Reply to Office action of March 2, 2007

6. The compounds tested were



C1

from the prior art and



11

according to the present invention.

7. The compounds were tested according to the assays described in the specification at pages 61-62.

8. The results are shown in the table below.

	IC <sub>50</sub> (nM) Breast MACL MCF7	IC <sub>50</sub> (nM) Renal RXF944L	IC <sub>50</sub> (nM) Lung 629L	IC <sub>50</sub> (nM) Melanoma MEXF462NL
C1	19.33	20.50	44.50	40.00
11	0.22	1.32	6.50	1.80

9. The data shows considerable improvement across a range of cell lines in the activity of compound 11 over compound C1, wherein the only change is in the 2-substituent from phenyl to naphthyl.

Appl. No. 10/534,825

Amdt. dated September 4, 2007

Reply to Office action of March 2, 2007

10. I hereby declare that all statements made herein of my own knowledge are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated this 31 day of August, 2007.

  
\_\_\_\_\_  
Dr. Phillip Howard

**Name:** Dr Philip Wilson Howard  
**DOB:** 24/6/1964  
**Age:** 42  
**Nationality:** British  
**Sex:** Male  
**Current Position:** Director of Chemistry Spirogen Senior Research Fellow,  
Deputy Director CR-UK Gene Targeted Drug Design  
Research Group

**Qualifications:**

BSc (2.1) Applied Chemistry, Kingston Polytechnic  
PhD University of East Anglia, "The preparation and  
Chemistry of Dihydrocatechol Derived Organoiron  
Complexes".

**Career:**

1991-1994 Post Doctoral Fellow, SmithKline Beecham  
1994-1995 Post Doctoral Fellow, University of  
Portsmouth  
1995-2000 Senior Lecturer, University of Portsmouth  
2000-2001 Senior Research Fellow, University of  
Nottingham  
2001-Director of Chemistry Spirogen/Senior Research  
Fellow ULSOP.

**Grants:**

CR-UK Programme Grant C180/A1060 (Co-PI)  
CR-UK Project Grant C180/A1066 (Co-PI)  
CR-UK Programme Grant C180/A5068 (Co-PI)  
CR-UK Studentship C180/A4522 (Co-PI)  
CR-UK Studentship C180/A2778 (Co-PI)  
EPSRC Case Award GR/PO1366/01 (Co-PI)  
EPSRC Case Award  
PSRC Quota Award  
CR-UK Equipment Grant C180/A3959 (Co-PI)

**Publications/patents:** Over 40 papers in peer reviewed scientific journals  
and over 14 patents (see below)

**Invited Lectures:**

SMi Drug Design, "Gene Targeting Approaches to Anti-  
Cancer Drug Design", London, UK (February 2003).

Societa Chimica Italiana Divisione Di Chimica Farmaceutica  
(Italian Medicinal Chemistry Summer School), Urbino, Italy  
(Jun-Jul 2003).

The Royal Society of Chemistry – Cancer Therapeutics in the  
21st Century, Manchester, UK (October 2003).

25th Winter Meeting of the EORTC-PAMM Group, Bradford, UK (January 2004).

Part 1 of SMI's Global Cancer Event - Innovations in Cancer Drug Discovery, "Design of Small Sequence-Selective DNA-Interactive Molecules", London, UK (June, 2004).

British Association of Cancer Research, Oxford, UK.

## Publications and Patents

### Papers

Masterson, Luke A.; Spanswick, Victoria J.; Hartley, John A.; Begent, Richard H.; Howard, Philip W.; Thurston, David E. **Synthesis and biological evaluation of novel pyrrolo[2,1-c][1,4]benzodiazepine prodrugs for use in antibody-directed enzyme prodrug therapy.** *Bioorganic & Medicinal Chemistry Letters* (2006), 16(2), 252-256. CODEN: BMCLE8 ISSN:0960-894X. CAN 144:150340 AN 2005:1251578 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Tiberghien, Arnaud C.; Hagan, David; Howard, Philip W.; Thurston, David E. **Application of the Stille coupling reaction to the synthesis of C2-substituted endo-exo unsaturated pyrrolo[2,1-c][1,4]benzodiazepines (PBDs).** *Bioorganic & Medicinal Chemistry Letters* (2004), 14(20), 5041-5044. CODEN: BMCLE8 ISSN:0960-894X. CAN 141:410907 AN 2004:767272 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Alley, Michael C.; Hollingshead, Melinda G.; Pacula-Cox, Christine M.; Waud, William R.; Hartley, John A.; Howard, Philip W.; Gregson, Stephen J.; Thurston, David E.; Sausville, Edward A. **SJG-136 (NSC 694501), A Novel Rationally Designed DNA Minor Groove Interstrand Cross-Linking Agent with Potent and Broad Spectrum Antitumor Activity: Part 2: Efficacy Evaluations.** *Cancer Research* (2004), 64(18), 6700-6706. CODEN: CNREA8 ISSN:0008-5472. CAN 141:271174 AN 2004:757703 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Hartley, John A.; Spanswick, Victoria J.; Brooks, Natalie; Clingen, Peter H.; McHugh, Peter J.; Hochhauser, Daniel; Pedley, R. Barbara; Kelland, Lloyd R.; Alley, Michael C.; Schultz, Robert; Hollingshead, Melinda G.; Schweikart, Karen M.; Tomaszewski, Joseph E.; Sausville, Edward A.; Gregson, Stephen J.; Howard, Philip W.; Thurston, David E. **SJG-136 (NSC 694501), a Novel Rationally Designed DNA Minor Groove Interstrand Cross-Linking Agent with Potent and Broad Spectrum Antitumor Activity: Part 1: Cellular Pharmacology, In vitro and Initial In vivo Antitumor Activity.** *Cancer Research* (2004), 64(18), 6693-6699. CODEN: CNREA8 ISSN:0008-5472. CAN 141:271173 AN 2004:757702 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Wilkinson, Gary P.; Taylor, James P.; Shnyder, Steve; Cooper, Patricia; Howard, Phil W.; Thurston, David E.; Jenkins, Terence C.; Loadman, Paul M. **Preliminary pharmacokinetic and bioanalytical studies of SJG-136 (NSC 694501), a sequence-selective pyrrolobenzodiazepine dimer DNA-cross-linking agent.** *Investigational New Drugs* (2004), 22(3), 231-240. CODEN: INNDDK ISSN:0167-6997. CAN 142:173 AN 2004:359111 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Chen, Zhizhi; Gregson, Stephen J.; Howard, Philip W.; Thurston, David E. **A novel approach to the synthesis of cytotoxic C2-C3 unsaturated pyrrolo[2,1-c]benzodiazepines (PBDs) with conjugated acrylyl C2-substituents.** *Bioorganic & Medicinal Chemistry Letters* (2004), 14(6), 1547-1549. CODEN: BMCLE8 ISSN:0960-894X. CAN 140:406790 AN 2004:189175 CAPLUS (Copyright

(C) 2006 ACS on SciFinder (R))

Masterson, Luke A.; Croker, Stephen J.; Jenkins, Terence C.; Howard, Philip W.; Thurston, David E. **Synthesis and biological evaluation of pyrrolo[2,1-c][1,4]benzodiazepine (PBD) C8 cyclic amine conjugates.** *Bioorganic & Medicinal Chemistry Letters* (2004), 14(4), 901-904. CODEN: BMCLE8 ISSN:0960-894X. CAN 140:321339 AN 2004:99276 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, Stephen J.; Howard, Philip W.; Gullick, Darren R.; Hamaguchi, Anzu; Corcoran, Kathryn E.; Brooks, Natalie A.; Hartley, John A.; Jenkins, Terence C.; Patel, Sejal; Guille, Matthew J.; Thurston, David E. **Linker Length Modulates DNA Cross-Linking Reactivity and Cytotoxic Potency of C8/C8' Ether-Linked C2-exo-Unsaturated Pyrrolo[2,1-c][1,4]benzodiazepine (PBD) Dimers.** *Journal of Medicinal Chemistry* (2004), 47(5), 1161-1174. CODEN: JMCMAR ISSN:0022-2623. CAN 140:280775 AN 2004:79123 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Hardy, Alison; Berry, Jane M.; Brooks-Turner, Natalie; Howard, Philip W.; Hartley, John A.; Thurston, David E. **The generation and DNA-interaction of PBD and CBI libraries.** *Small Molecule DNA and RNA Binders* (2003), 2 697-710. CODEN: 69EKGK CAN 140:370949 AN 2003:679629 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Kang, Gyoung-Dong; Howard, Philip W.; Thurston, David E. **Synthesis of a novel C2-aryl substituted 1,2-unsaturated pyrrolobenzodiazepine.** *Chemical Communications (Cambridge, United Kingdom)* (2003), (14), 1688-1689. CODEN: CHCOFS ISSN:1359-7345. CAN 140:42146 AN 2003:496748 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, Stephen J.; Howard, Philip W.; Thurston, David E. **Synthesis of the first examples of A-C8/C-C2 amide-Linked pyrrolo[2,1-c][1,4]benzodiazepine dimers.** *Bioorganic & Medicinal Chemistry Letters* (2003), 13(14), 2277-2280. CODEN: BMCLE8 ISSN:0960-894X. CAN 139:261068 AN 2003:485873 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Cooper, Nectaroula; Hagan, David R.; Tiberghien, Arnaud; Ademefun, Temitope; Matthews, Charles S.; Howard, Philip W.; Thurston, David E. **Synthesis of novel C2-aryl pyrrolobenzodiazepines (PBDs) as potential antitumor agents.** *Chemical Communications (Cambridge, United Kingdom)* (2002), (16), 1764-1765. CODEN: CHCOFS ISSN:1359-7345. CAN 138:122628 AN 2002:557716 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Berry, Jane M.; Howard, Philip W.; Kelland, Lloyd R.; Thurston, David E. **Synthesis and biological evaluation of an N10-Psec substituted pyrrolo[2,1-c][1,4]benzodiazepine prodrug.** *Bioorganic & Medicinal Chemistry Letters* (2002), 12(10), 1413-1416. CODEN: BMCLE8 ISSN:0960-894X. CAN 137:247674 AN 2002:324912 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, S. J.; Howard, P. W.; Corcoran, K. E.; Jenkins, T. C.; Kelland, L. R.; Thurston, D. E. **Synthesis of the first example of a C2-C3/C2'-C3'-endo unsaturated pyrrolo[2,1-c][1,4]benzodiazepine dimer.** *Bioorganic & Medicinal Chemistry Letters* (2001), 11(21), 2859-2862. CODEN: BMCLE8 ISSN:0960-894X. CAN 136:200170 AN 2001:746612 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, Stephen J.; Howard, Philip W.; Hartley, John A.; Brooks, Natalie A.; Adams, Lesley J.; Jenkins, Terence C.; Kelland, Lloyd R.; Thurston, David E. **Design, synthesis, and evaluation of a novel pyrrolobenzodiazepine DNA-interactive agent with highly efficient cross-linking ability and potent cytotoxicity.** *Journal of Medicinal Chemistry* (2001), 44(5), 737-748. CODEN: JMCMAR ISSN:0022-2623. CAN 134:260871 AN 2001:68712 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Sagnou, M. J.; Howard, P. W.; Gregson, S. J.; Eno-Amooquaye, E.; Burke, P. J.; Thurston, D. E. **Design and synthesis of novel pyrrolobenzodiazepine (PBD) prodrugs for ADEPT and GDEPT.** *Bioorganic & Medicinal Chemistry Letters* (2000), 10(18), 2083-2086. CODEN: BMCLE8 ISSN:0960-894X. CAN 133:362758 AN 2000:619247 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, S. J.; Howard, P. W.; Barcella, S.; Nakanya, A.; Jenkins, T. C.; Kelland, L. R.; Thurston, D. E. **Effect of C2/C3-endo unsaturation on the cytotoxicity and DNA-binding reactivity of pyrrolo[2,1-c][1,4]benzodiazepines.** *Bioorganic & Medicinal Chemistry Letters* (2000), 10(16), 1849-1851. CODEN: BMCLE8 ISSN:0960-894X. CAN 133:321863 AN 2000:565893 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, Stephen J.; Howard, Philip W.; Corcoran, Kathryn E.; Barcella, Simona; Yasin, Maqsood M.; Hurst, Abigail A.; Jenkins, Terence C.; Kelland, Lloyd R.; Thurston, David E. **Effect of C2-exo unsaturation on the cytotoxicity and DNA-binding reactivity of pyrrolo[2,1-c][1,4]benzodiazepines.** *Bioorganic & Medicinal Chemistry Letters* (2000), 10(16), 1845-1847. CODEN: BMCLE8 ISSN:0960-894X. CAN 133:309885 AN 2000:565892 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Berry, J. M.; Howard, P. W.; Thurston, D. E. **Solid-phase synthesis of DNA-interactive pyrrolo[2,1-c][1,4]benzodiazepines.** *Tetrahedron Letters* (2000), 41(32), 6171-6174. CODEN: TELEAY ISSN:0040-4039. CAN 133:281765 AN 2000:528841 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Baraldi, Pier Giovanni; Balboni, Gianfranco; Cacciari, Barbara; Guiotto, Andrea; Manfredini, Stefano; Romagnoli, Romeo; Spalluto, Giampiero; Thurston, David E.; Howard, Philip W.; Bianchi, Nicoletta; Rutigliano, Cristina; Mischianti, Carlo; Gambari, Roberto. **Synthesis, in Vitro Antiproliferative Activity, and DNA-Binding Properties of Hybrid Molecules Containing Pyrrolo[2,1-c][1,4]benzodiazepine and Minor-Groove-Binding Oligopyrrole Carriers.** *Journal of Medicinal Chemistry* (1999), 42(25), 5131-5141. CODEN: JMCMAR ISSN:0022-2623. CAN 132:137361 AN 1999:758546 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Wilson, Stuart C.; Howard, Philip W.; Forrow, Stephen M.; Hartley, John A.; Adams, Lesley J.; Jenkins, Terence C.; Kelland, Lloyd R.; Thurston, David E. **Design, Synthesis, and Evaluation of a Novel Sequence-Selective Epoxide-Containing DNA Cross-Linking Agent Based on the Pyrrolo[2,1-c][1,4]benzodiazepine System.** *Journal of Medicinal Chemistry* (1999), 42(20), 4028-4041. CODEN: JMCMAR ISSN:0022-2623. CAN 132:89603 AN 1999:583940 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Thurston, David E.; Bose, D. Subhas; Howard, Philip W.; Jenkins, Terence C.; Leoni, Alberto; Baraldi, Pier G.; Guiotto, Andrea; Cacciari, Barbara; Kelland, Lloyd R.; Foloppe, Marie-Paule; Rault, Sylvain. **Effect of A-ring modifications on the DNA-binding behavior and cytotoxicity of pyrrolo[2,1-c][1,4]benzodiazepines.** *Journal of Medicinal Chemistry* (1999), 42(11), 1951-1964. CODEN: JMCMAR ISSN:0022-2623. CAN 131:18989 AN 1999:304467 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Gregson, Stephen J.; Howard, Philip W.; Thurston, David E.; Jenkins, Terence C.; Kelland, Lloyd R. **Synthesis of a novel C2/C2'-exo unsaturated pyrrolobenzodiazepine cross-linking agent with remarkable DNA binding affinity and cytotoxicity.** *Chemical Communications (Cambridge)* (1999), (9), 797-798. CODEN: CHCOFS ISSN:1359-7345. CAN 131:116218 AN 1999:273645 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Baraldi, Pier Giovanni; Cacciari, Barbara; Guiotto, Andrea; Leoni, Alberto; Romagnoli, Romeo; Spalluto, Giampiero; Mongelli, Nicola; Howard, Philip W.; Thurston, David E.; Bianchi, Nicoletta; Gambari, Roberto. **Design, synthesis and biological activity of a pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid.** *Bioorganic & Medicinal Chemistry Letters* (1998), 8(21), 3019-3024. CODEN: BMCLE8 ISSN:0960-894X. CAN 130:95405 AN 1998:760824 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Guiotto, Andrea; Howard, Philip W.; Baraldi, Pier Giovanni; Thurston, David E. **Synthesis of novel C7-aryl substituted pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) via pro-N10-Troc protection and Suzuki coupling.** *Bioorganic & Medicinal Chemistry Letters* (1998), 8(21), 3017-3018. CODEN: BMCLE8 ISSN:0960-894X. CAN 130:95540 AN 1998:760823 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Kamal, Ahmed; Howard, Philip W.; Reddy, B. S. Narayan; Reddy, B. S. Praveen; Thurston, David E. **Synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics: oxidation of cyclic secondary amine with TPAP.** *Tetrahedron* (1997), 53(9), 3223-3230. CODEN: TETRAB ISSN:0040-4020. CAN 126:225131 AN 1997:165424 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Thurston, David E.; Bose, D. Subhas; Thompson, Andrew S.; Howard, Philip W.; Leoni, Alberto; Croker, Stephen J.; Jenkins, Terrence C.; Neidle, Steven; Hartley, John A.; Hurley, Laurence H. **Synthesis of Sequence-Selective C8-Linked Pyrrolo[2,1-c][1,4]benzodiazepine Interstrand DNA Crosslinking Agents.** *Journal of Organic Chemistry* (1996), 61(23), 8141-8147. CODEN: JOCEAH ISSN:0022-3263. CAN 126:8088 AN 1996:644058 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howell, James A. S.; Bell, Andrew G.; O'Leary, Paula J.; Stephenson, G. Richard; Hastings, Michelle; Howard, Philip W.; Owen, David A.; Whitehead, Andrew J.; McArdle, Patrick; Cunningham, Desmond. **Synthesis and Reactivity of Cyclic and Acyclic [(1-(acyloxy)cyclopentadienyl)Fe(CO)2L]X and [(1-alkoxypentadienyl)Fe(CO)2L]X Salts (L = CO, PPh3).** *Organometallics* (1996), 15(20), 4247-4257. CODEN: ORGND7 ISSN:0276-7333. CAN 125:248038 AN 1996:551059 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Zioga, G.; Howard, P. W.; Canfield, L. M.; Gescher, A.; Thurston, D. E. **Interaction of the pyrrolobenzodiazepine antitumor agent anthramycin with glutathione: a possible role in metabolism.** *Pharmaceutical Sciences* (1996), 2(1), 39-42. CODEN: PHSCFB ISSN:1356-6881. CAN 125:211697 AN 1996:495794 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Wilson, Stuart C.; Howard, Philip W.; Thurston, David E. **Design and synthesis of a novel epoxide-containing pyrrolo[2,1-c][1,4]benzodiazepine (PBD) via a new cyclization procedure.** *Electronic Conference on Trends in Organic Chemistry [CD-ROM]* (1996), Meeting Date 1995, Paper 32. CODEN: 62TKAB CAN 125:33599 AN 1996:247427 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Wilson, Stuart C.; Howard, Philip W.; Thurston, David E. **Design and synthesis of a novel epoxide-containing pyrrolo[2,1-c][1,4]benzodiazepine (PBD) via a new cyclization procedure.** *Tetrahedron Letters* (1995), 36(35), 6333-6. CODEN: TELEAY ISSN:0040-4039. CAN 124:8772 AN 1995:786320 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Stephenson, G. Richard; Howard, Philip W.. **Circular dichroism spectra of tricarbonyliron  $\pi$ -complexes.** *Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry* (1972-1999) (1994), (19), 2873-80. CODEN: JCPRB4 ISSN:0300-922X. CAN 122:56167 AN 1995:133777 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip Wilson. **The preparation and chemistry of dihydrocatechol derived organoiron complexes.** (1991), 280 pp. CAN 118:169287 AN 1993:169287 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Stephenson, G. Richard; Astley, Stephen T.; Palotai, Ian M.; Howard, Philip W.; Owen, David A.; Williams, Sarah. **Regiocontrolled applications of transition metal  $\pi$ -complexes.** *Org. Synth. Organomet., Proc. Symp., 3rd* (1991), Meeting Date 1990, 169-85. CODEN: 57ODAN CAN 116:59591 AN 1992:59591 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Stephenson, G. Richard; Howard, Philip W.; Taylor, Stephen C. **Regioselective access to tricarbonyliron complexes: controlled preparation and reactions of trifluoromethyl substituted complexes.** *Journal of Organometallic Chemistry* (1991), 419(1-2), C14-C17. CODEN: JORCAI ISSN:0022-328X. CAN 116:59587 AN 1992:59587 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Stephenson, G. Richard; Howard, Philip W.; Owen, David A.; Whitehead, Andrew J. **Complementary regioselection in nucleophile additions to cationic  $\pi$  5-cyclohexadienyliron complexes.** *Journal of the Chemical Society, Chemical Communications* (1991), (9), 641-2. CODEN: JCCCAT ISSN:0022-4936. CAN 115:49913 AN 1991:449913 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))



2006 ACS on SciFinder (R))

Stephenson, G. Richard; Howard, Philip W.; Taylor, Stephen C. **Assignment of absolute configurations from the circular dichroism spectra of cyclic  $\square$  4-diene complexes of iron tricarbonyl.** Journal of the Chemical Society, Chemical Communications (1991), (2), 127-9. CODEN: JCCCAT ISSN:0022-4936. CAN 114:164447 AN 1991:164447 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip W.; Stephenson, G. Richard; Taylor, Stephen C. **Evidence for an anomalous microbial oxidation of acetophenone: new access to optically active tricarbonyliron complexes.** Journal of the Chemical Society, Chemical Communications (1990), (17), 1182-4. CODEN: JCCCAT ISSN:0022-4936. CAN 113:208060 AN 1990:608060 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip W.; Stephenson, G. Richard; Taylor, Stephen C. **Transition metal mediated asymmetric synthesis. X. Homochiral  $\square$ -complexes with planar chirality: synthetic equivalents of chiral cyclohexadiene dications.** Journal of Organometallic Chemistry (1989), 370(1-3), 97-109. CODEN: JORCAI ISSN:0022-328X. CAN 112:179353 AN 1990:179353 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip W.; Stephenson, G. Richard; Taylor, Stephen C. **Convenient access to homochiral tricarbonyliron complexes.** Journal of the Chemical Society, Chemical Communications (1988), (24), 1603-4. CODEN: JCCCAT ISSN:0022-4936. CAN 111:195011 AN 1989:595011 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Stephenson, G. R.; Alexander, R. P.; Morley, C.; Howard, P. W..  **$\square$ -Complexes with planar chirality: control centers for stereoselective synthesis.** Philosophical Transactions of the Royal Society of London, Series A: Mathematical, Physical and Engineering Sciences (1988), 326(1592), 545-56. CODEN: PTRMAD ISSN:0080-4614. CAN 111:57790 AN 1989:457790 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip W.; Stephenson, G. Richard; Taylor, Stephen C. **Transition metal mediated asymmetric synthesis. VII. 6-Methoxycyclohexadienyliron complexes: access to synthetic equivalents of cyclohexadiene dications.** Journal of Organometallic Chemistry (1988), 339(3), C5-C8. CODEN: JORCAI ISSN:0022-328X. CAN 110:39122 AN 1989:39122 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

## Patents

Howard, Philip Wilson; Gregson, Stephen John; Taylor, Peter William; Thurston, David Edwin; Hadjivassileva, Tsveta Stepanova. **Preparation, DNA crosslinking reactivity, antitumor and antibacterial activity of pyrrolbenzodiazepine dimers.** PCT Int. Appl. (2005), 62 pp. CODEN: PIXXD2 WO 2005085260 A1 20050915 CAN 143:306350 AN 2005:1004755 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip Wilson; Kang, Gyoung-Dong. **Preparation, DNA crosslinking reactivity and antiproliferative activity of pyrrolbenzodiazepine dimers.** PCT Int. Appl. (2005), 108 pp. CODEN: PIXXD2 WO 2005085259 A2 20050915 CAN 143:306349 AN 2005:1004754 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip Wilson; Gregson, Stephen John. **Preparation of pyrrolbenzodiazepinone derivatives as antitumor agents.** PCT Int. Appl. (2005), 88 pp. CODEN: PIXXD2 WO 2005085251 A1 20050915 CAN 143:306348 AN 2005:1004748 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

Howard, Philip Wilson; Gregson, Stephen John; Tiberghien, Arnaud Charles. **Preparation of C8/C8' linked 5-oxo-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c]-1,4-benzodiazepine dimers with 1H-pyrroledicarboxylic acid amide linkers and oligomeric analogs thereof as well as related compounds for**

**the treatment of proliferative diseases.** PCT Int. Appl. (2005), 108 pp. CODEN: PIXXD2 WO 2005085250 A1 20050915 CAN 143:306347 AN 2005:1004747 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Howard, Philip Wilson; Wells, Geoffrey. Preparation of aminobiaryl carboxylic acids for the manufacture of medicaments for treating proliferative disease.** PCT Int. Appl. (2005), 90 pp. CODEN: PIXXD2 WO 2005085177 A2 20050915 CAN 143:286420 AN 2005:1004692 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Howard, Philip Wilson; Thurston, David Edwin; Gregson, Stephen John. Preparation, DNA crosslinking reactivity and antitumor activity of pyrrolobenzodiazepines.** PCT Int. Appl. (2005), 24 pp. CODEN: PIXXD2 WO 2005042535 A1 20050512 CAN 142:463770 AN 2005:409522 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Vishnuvajjala, B. Rao; Liu, Paul S.; Snader, Kenneth M.; Thurston, David; Howard, Philip W.; Turner, Gregory. Method for preparation of pyrrolobenzodiazepine derivatives and compositions comprising them.** PCT Int. Appl. (2005), 89 pp. CODEN: PIXXD2 WO 2005040170 A2 20050506 CAN 142:447059 AN 2005:395315 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Howard, Philip; Masterson, Luke. Synthesis of protected pyrrolobenzodiazepines.** PCT Int. Appl. (2005), 120 pp. CODEN: PIXXD2 WO 2005023814 A1 20050317 CAN 142:316867 AN 2005:238991 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Thurston, David Edwin; Howard, Philip Wilson. Preparation of pyrrolobenzodiazepines as anticancer agents.** PCT Int. Appl. (2004), 74 pp. CODEN: PIXXD2 WO 2004043963 A1 20040527 CAN 140:423715 AN 2004:430806 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Thurston, David Edwin; Howard, Philip Wilson. Preparation of cyclopropylindole derivatives and peptide libraries containing them.** PCT Int. Appl. (2001), 69 pp. CODEN: PIXXD2 WO 2001016104 A1 20010308 CAN 134:208138 AN 2001:167967 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Thurston, David Edwin; Howard, Philip Wilson. Solid-phase preparation and combinatorial libraries of pyrrolobenzodiazepine derivatives for drug screening.** PCT Int. Appl. (2000), 65 pp. CODEN: PIXXD2 WO 2000012509 A2 20000309 CAN 132:207852 AN 2000:161285 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Thurston, David Edwin; Howard, Philip Wilson. Preparation of pyrrolobenzodiazepines (PBDs) as antitumor agents.** PCT Int. Appl. (2000), 258 pp. CODEN: PIXXD2 WO 2000012508 A2 20000309 CAN 132:207851 AN 2000:161284 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Thurston, David Edwin; Howard, Philip Wilson. Preparation of pyrrolobenzodiazepines (PBDs) as antitumor antibiotics.** PCT Int. Appl. (2000), 101 pp. CODEN: PIXXD2 WO 2000012507 A2 20000309 CAN 132:207703 AN 2000:161283 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))

**Thurston, David Edwin; Howard, Philip Wilson. Preparation of peptidyl pyrrolobenzodiazepines as pharmaceuticals.** PCT Int. Appl. (2000), 158 pp. CODEN: PIXXD2 WO 2000012506 A2 20000309 CAN 132:208134 AN 2000:161282 CAPLUS (Copyright (C) 2006 ACS on SciFinder (R))